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What is claimed is:

- 10 *heli G37*
1. A method of inhibiting activation by CD40 ligand of cells bearing CD40 on the cell surface, other than B cells, comprising contacting the cells with an agent capable of inhibiting interaction between CD40 ligand and the cells, in an amount effective to inhibit activation of the cells.
 - 15 2. The method of claim 1, wherein the CD40-bearing cells are selected from the group consisting of fibroblasts, endothelial cells, epithelial cells, T cells, basophils, macrophages, Reed-Steinberg cells, and dendritic cells.
 - 20 3. The method of claim 2, wherein the epithelial cells are keratinocytes.
 - 25 4. The method of claim 1, wherein the agent inhibits binding of CD40 ligand to CD40 on the cells.
 5. The method of claim 1, wherein the agent is a protein.
 - 30 6. The method of claim 5, wherein the protein comprises an antibody or portion thereof.
 7. The method of claim 6, wherein the antibody is a monoclonal antibody.
 - 35 8. The method of claim 7, wherein the monoclonal antibody is a chimeric antibody.
 - 40 9. The method of claim 7, wherein the monoclonal antibody is a humanized antibody.

- 5 10. The method of claim 7, wherein the monoclonal antibody is a primatized antibody.
11. The method of claim 6, wherein the portion of the antibody comprises a complementarity determining region or variable region of a light or heavy chain.
- 10 12. The method of claim 6, wherein the portion of the antibody comprises a complementarity determining region or a variable region.
- 15 13. The method of claim 12, wherein the portion of the antibody comprises a Fab, or a single chain antibody.
- 20 14. The method of claim 5, wherein the protein comprises soluble extracellular region of CD40 ligand, or variants thereof including conservativ substituents, or portion thereof; or soluble extracellular region of CD40, or variants thereof
- 25 including conservative substituents, or portion thereof.
15. The method of claim 14, wherein the solubl extracellular region of CD40 ligand or CD40 is a monomer.
- 30 16. The method of claim 14, wherein the solubl extracellular region of CD40 is an oligomer.
- 35 17. The method of claim 14, wherein the protein comprising soluble extracellular region of CD40 or portion thereof further comprises an Fc region fused to the extracellular region of CD40 or portion thereof.
- 40 18. The method of claim 17, wherein th Fc region is

- 5 capable of binding to protein A or protein G.
19. The method of claim 17, wherein the Fc region
comprises IgG, IgA, IgM, IgD, or IgE, or subclasses
thereof.
- 10
- 20 The method of claim 19, wherein:
 the IgG is IgG₁, IgG₂, IgG₃, or IgG₄; or
 the IgA is IgA₁ or IgA₂.
- 15 21. The method of claim 1, wherein the agent
specifically binds to the antigen to which
monoclonal antibody 5c8 (ATCC Accession No. HB
10916) specifically binds.
- 20 22. The method of claim 21, wherein the agent is an
antibody.
23. The method of claim 22, wherein the antibody is
monoclonal antibody 5c8 (ATCC Accession No. HB
25 10916).
24. The method of claim 1, wherein the agent is a small
molecule.
- 30 25. The method of claim 1, wherein the agent
specifically binds to CD40 on the cell surface.
26. The method of claim 25, wherein the agent is a
protein.
- 35 27. The method of claim 26, wherein the protein is an
antibody.
28. The method of claim 27, wherein the antibody is a
40 monoclonal antibody.

- 5 29. The method of claim 28, wherein the monoclonal antibody is chimeric, humanized, or primatized.
30. The method of claim 26, wherein the protein comprises the extracellular region of CD40 ligand.
- 10 31. The method of claim 1, wherein the agent is nonprotein.
32. The method of claim 1, wherein the agent is selected from a library of known agents.
- 15 33. The method of claim 1, wherein the agent is modified from a known agent.
- 20 34. The method of claim 33, wherein the modified agent is designed by structure optimization of a lead inhibitory agent based on a three-dimensional structure of a complex of soluble extracellular region of CD40 ligand or portion thereof with the lead inhibitory agent.
- 25 35. The method of claim 1, wherein the agent is selected by a screening method, which comprises:
- 30 isolating a sample of cells;
- culturing the sample under conditions permitting activation of CD40-bearing cells;
- 35 contacting the sample with cells expressing a protein which is specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916, or with a protein which is specifically recognized by
- 40 monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916, effective to

5 activate the CD40-bearing cells;

contacting the sample with an amount of the agent
effective to inhibit activation of the CD40-bearing
cells if the agent is capable of inhibiting
10 activation of the CD40-bearing cells; and

determining whether the cells expressing the protein
which is specifically recognized by monoclonal
antibody 5c8 produced by the hybridoma having ATCC
15 Accession No. HB 10916, or with the protein which is
specifically recognized by monoclonal antibody 5c8
produced by the hybridoma having ATCC Accession No.
HB 10916, activate the CD40-bearing cells in the
presence of the agent.

20 36. The method of claim 35, wherein the agent is
selected from a library of known agents.

25 37. The method of claim 36, wherein the known agents are
nonprotein agents.

30 38. A method of inhibiting activation by CD40 ligand of
cells bearing CD40 on the cell surface, other than
B cells, in a subject, comprising administering to
the subject an agent capable of inhibiting
interaction between CD40 ligand and the cells, in an
amount effective to inhibit activation of the cells
in the subject.

35 39. The method of claim 38, wherein the CD40-bearing
cells are selected from the group consisting of
fibroblasts, endothelial cells, epithelial cells, T
cells, basophils, macrophages, Reed-Steinberg cells,
40 and dendritic cells.

- 5 40. The method of claim 39, wherein the epithelial cells are keratinocytes.
41. The method of claim 38, wherein the agent inhibits binding of CD40 ligand to CD40 on the cells.
- 10 42. The method of claim 38, wherein the agent is a protein.
43. The method of claim 42, wherein the protein comprises an antibody or portion thereof.
- 15 44. The method of claim 43, wherein the antibody is a monoclonal antibody.
- 20 45. The method of claim 43, wherein the monoclonal antibody is a chimeric antibody.
46. The method of claim 44, wherein the monoclonal antibody is a humanized antibody.
- 25 47. The method of claim 44, wherein the monoclonal antibody is a primatized antibody.
48. The method of claim 43, wherein the portion of the antibody comprises a complementarity determining region or variable region of a light or heavy chain.
- 30 49. The method of claim 43, wherein the portion of the antibody comprises a complementarity determining region or a variable region.
- 35 50. The method of claim 49, wherein the portion of the antibody comprises a Fab, or a single chain antibody.
- 40 51. The method of claim 38, wherein the agent

- 5 specifically binds to the antigen to which
monoclonal antibody 5c8 (ATCC Accession No. HB
10916) specifically binds.
- 10 52 The method of claim 51, wherein the agent is an
antibody.
53. The method of claim 52, wherein the antibody is
monoclonal antibody 5c8 (ATCC Accession No. HB
10916).
- 15 54. The method of claim 38, wherein the subject is a
mammal.
- 20 55. The method of claim 54, wherein the mammalian
subject is a human.
56. The method of claim 54, wherein the mammalian
subject is a rodent.
- 25 57. The method of claim 38, wherein the protein
comprises soluble extracellular region of CD40
ligand, or variants thereof including conservative
substituents, or portion thereof; or soluble
30 extracellular region of CD40, or variants thereof
including conservative substituents, or portion
thereof.
- 35 58. The method of claim 57, wherein the soluble
extracellular region of CD40 ligand or CD40 is a
monomer.
59. The method of claim 57, wherein the soluble
extracellular region of CD40 is an oligomer.
- 40 60. The method of claim 57, wherein the protein
comprising soluble extracellular region of CD40 or

- 5 portion thereof further comprises an Fc region fused
to the extracellular region of CD40 or portion
thereof.
61. The method of claim 60, wherein the Fc region is
10 capable of binding to protein A or protein G.
62. The method of claim 60, wherein the Fc region
comprises IgG, IgA, IgM, IgD, or IgE, or subclasses
thereof.
- 15 63. The method of claim 62, wherein:
 the IgG is IgG₁, IgG₂, IgG₃, or IgG₄; or
 the IgA is IgA₁ or IgA₂.
- 20 64. The method of claim 38, wherein the agent is a small
molecule.
65. The method of claim 38, wherein the agent
specifically binds to CD40 on the cell surface.
- 25 66. The method of claim 65, wherein the agent is a
protein.
67. The method of claim 66, wherein the protein is an
30 antibody.
68. The method of claim 67, wherein the antibody is a
monoclonal antibody.
- 35 69. The method of claim 68, wherein the monoclonal
antibody is chimeric, humanized, or primatized.
70. The method of claim 66, wherein the protein
comprises the extracellular region of CD40 ligand.
- 40 71. Th method of claim 38, wher in the ag nt is

5 nonprotein.

72. The method of claim 38, wherein the agent is selected from a library of known agents.

10 73. The method of claim 38, wherein the agent is modified from a known agent.

15 74. The method of claim 73 wherein the modified agent is designed by structure optimization of a lead inhibitory agent based on a three-dimensional structure of a complex of soluble extracellular region of CD40 ligand or portion thereof with the lead inhibitory agent.

20 75. The method of claim 38, wherein the agent is selected by a screening method, which comprises:

isolating a sample of cells;

25 culturing the sample under conditions permitting activation of CD40-bearing cells;

30 contacting the sample with cells expressing a protein which is specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916, or with a protein which is specifically recognized by monoclonal antibody 5c8 produced by the hybridoma having ATCC Accession No. HB 10916, effective to activate the CD40-bearing cells;

35 contacting the sample with an amount of the agent effective to inhibit activation of the CD40-bearing cells if the agent is capable of inhibiting activation of the CD40-bearing cells; and
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- 5 determining whether the cells expressing the protein
which is specifically recognized by monoclonal
antibody 5c8 produced by the hybridoma having ATCC
Accession No. HB 10916, or with the protein which is
specifically recognized by monoclonal antibody 5c8
10 produced by the hybridoma having ATCC Accession No.
HB 10916, activate the CD40-bearing cells in the
presence of the agent.
- 15 76. The method of claim 75, wherein the agent is
selected from a library of known agents.
77. The method of claim 76, wherein the known agents are
nonprotein agents.
- 20 78. A method of inhibiting an inflammatory response in
a subject, comprising the method of claim 38.
79. A method of treating a condition dependent on CD40
ligand-induced activation of fibroblast cells in a
25 subject, comprising the method of claim 38.
80. The method of claim 79, wherein the fibroblasts are
synovial membrane fibroblasts, dermal fibroblasts,
30 pulmonary fibroblasts, or liver fibroblasts.
81. The method of claim 79, wherein the condition is
selected from the group consisting of arthritis,
scleroderma, and fibrosis.
- 35 82. The method of claim 81, wherein the arthritis is
rheumatoid arthritis, non-rheumatoid inflammatory
arthritis, arthritis associated with Lyme disease,
or osteoarthritis.
- 40 83. The method of claim 81, wherein the fibrosis is

- 5 pulmonary fibrosis, hypersensitivity pulmonary
fibrosis, or a pneumoconiosis.
84. The method of claim 83, wherein the pulmonary
10 fibrosis is pulmonary fibrosis secondary to adult
respiratory distress syndrome, drug-induced
pulmonary fibrosis, idiopathic pulmonary fibrosis,
or hypersensitivity pneumonitis.
85. The method of claim 83, wherein the pneumoconiosis
15 is asbestosis, siliconosis, or Farmer's lung.
86. The method of claim 81, wherein the fibrosis is a
fibrotic disease of the liver or lung.
- 20 87. The method of claim 86, wherein the fibrotic disease
of the lung is caused by rheumatoid arthritis or
scleroderma.
88. The method of claim 86, wherein the fibrotic disease
25 of the liver is selected from the group consisting
of:
Hepatitis-C;
Hepatitis-B;
cirrhosis;
30 cirrhosis of the liver secondary to a toxic
insult;
cirrhosis of the liver secondary to drugs;
cirrhosis of the liver secondary to a viral
infection; and
35 cirrhosis of the liver secondary to an
autoimmune disease.
89. The method of claim 88, wherein the toxic insult is
alcohol consumption.
- 40 90. The method of claim 88, wherein the viral infection

- 5 is Hepatitis B, Hepatitis C, or hepatitis non-B non-C.
91. The method of claim 88, wherein the autoimmune disease is primary biliary cirrhosis, or Lupoid hepatitis.
- 10
92. A method of treating a condition dependent on CD40 ligand-induced activation of endothelial cells in a subject, comprising the method of claim 38.
- 15
93. The method of claim 92, wherein the condition is selected from the group consisting of atherosclerosis, reperfusion injury, allograft rejection, organ rejection, and chronic inflammatory autoimmune diseases.
- 20
94. The method of claim 93, wherein the atherosclerosis is accelerated atherosclerosis associated with organ transplantation.
- 25
95. The method of claim 93, wherein the chronic inflammatory autoimmune disease is vasculitis, rheumatoid arthritis, scleroderma, or multiple sclerosis.
- 30
96. A method of treating a condition dependent on CD40 ligand-induced activation of epithelial cells in a subject, comprising the method of claim 38.
- 35
97. The method of claim 96 wherein the epithelial cells are keratinocytes, and the condition is psoriasis.
98. A method of inhibiting activation by CD40 ligand of myeloma cells bearing CD40 on the cell surface, comprising contacting the cells with an agent capable of inhibiting interaction between CD40
- 40

5 ligand and the cells, in an amount effective to
inhibit activation of the cells.

99. A method of inhibiting activation by CD40 ligand of
myeloma cells bearing CD40 on the cell surface, in
10 a subject, comprising administering to the subject
an agent capable of inhibiting interaction between
CD40 ligand and the cells, in an amount effective to
inhibit activation of the cells in the subject.

15 100. A method of treating a condition dependent on CD40
ligand-induced activation of myeloma cells in a
subject, comprising the method of inhibiting
activation by CD40 ligand of myeloma cells bearing
CD40 on the cell surface of claim 99.

20 101. The method of claim 100, wherein the condition is
multiple myeloma.

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